

Appl. No. 10/016,850
Reply to Office Action of October 18, 2004

Remarks

Introduction

The above-identified application has been carefully reviewed in light of the Office Action mailed October 18, 2004, which included a final rejection of the pending claims, and the Advisory Action mailed February 15, 2005. An initial Amendment to the Final Office Action was filed on January 18, 2005. The Amendment filed on January 18, 2005 was not entered. Therefore, the present claims have been amended in view of the Amendment filed on July 9, 2004. The present Amendment is being submitted with a Request for Continued Examination (RCE).

Claims 1-16 were pending, and claims 7 and 10 have been withdrawn from consideration. By way of this response, claims 1-6, 8, 9, 11, 12, and 14-16 have been amended and claim 13 has been cancelled, without prejudice. Support for the amendments to the claims can be found in the application as originally filed, and care has been taken to avoid adding new matter. Accordingly, claims 1-12 and 14-16 remain pending.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-6, 8, 9, and 11-16 remain rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification to enable a person of ordinary skill in the art to make or use the invention.

Applicant respectfully disagrees and traverses the rejection as it relates to the present claims.

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As acknowledged in the Advisory Action, the Examiner agrees that the specification is enabling for ophthalmic drops (paragraph 11 of the Advisory Action).

The present claims have been amended to make more clear that the present claims are directed to topical ophthalmic compositions comprising carriers and defined pharmaceutical conjugates. Applicant submits that the specification of the above-identified application, taken as a whole, discloses sufficient information to enable a person of ordinary skill in the art to make and use such topical ophthalmic compositions, for example, the ophthalmic drops disclosed in the examples. This is particularly true in view of the large body of prior art knowledge with regard to topical ophthalmic compositions and the high skill level of those of ordinary skill in the art. Limiting the present claims to ophthalmic drops would be an undue restriction on the scope of the present invention.

In view of the above, applicant submits that the present claims, and claims 1-6, 8, 9, 11, 12, and 14-16 in particular, are sufficiently enabled to comply with 35 U.S.C. § 112, first paragraph, and respectfully requests that the rejection of the present claims based on this statutory provision be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claim 8 remains rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for reciting the word "derivatives"

Claim 8 has been amended as set forth above to delete reference to "derivatives". As acknowledged in the Advisory

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Action (paragraph 5), the present amendments are sufficient to overcome the rejections under 35 U.S.C. § 112, second paragraph.

In view of the above, applicant submits that the present claims, that is claims 1-6, 8-9, 11, 12, and 14-16, are definite under 35 U.S.C. § 112, second paragraph, and respectfully requests that the rejection of the present claims based on this statutory provision be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 1-6, 8, 9, 11-13, 15, and 16 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Desantis Jr. (U.S. 2001/0047012; hereinafter Desantis) and Collins et al. (WO 01/92288; hereinafter Collins).

Applicant respectfully disagrees and traverses the rejection as it pertains to the present claims.

Applicant submits that the combination of Desantis and Collins does not disclose, teach, or suggest the present invention. For example, the combination of Desantis and Collins fails to disclose, teach, or even suggest a topical ophthalmic composition comprising a carrier and a pharmaceutical conjugate, which conjugate comprises a therapeutic component covalently coupled to an efficacy enhancing component having the formula A, as recited in the present claims.

Desantis does not disclose, teach, or suggest the present invention. For example, Desantis does not disclose, teach, or even suggest a topical ophthalmic composition comprising a carrier and a conjugate comprising a therapeutic component

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covalently coupled to an efficacy enhancing component, as recited in the present claims.

In direct contrast to the present claims, Desantis discloses that separate compounds in separate compositions are separately administered to a patient. Further, Desantis discloses that at least one of the compounds is administered orally (see paragraph 0019). In addition, Desantis discloses a method of treating a person which comprises administering at least one glutamate antagonist systemically, and at least one IOP-lowering composition topically to an affected eye (see paragraph 0032).

It is clear from the disclosure of Desantis that the glutamate antagonist and the IOP-lowering agent are separate from each other and are administered in separate compositions and by separate routes. Because the glutamate antagonist and the IOP-lowering agent are separate compounds, provided in separate compositions, and administered by separate routes, the glutamate antagonist and the IOP-lowering agent of Desantis are not in the form of a covalently coupled conjugate or even in a single topical ophthalmic composition, as recited in the present claims.

In view of the separate agents in separate compositions administered by separate routes taught by Desantis, applicant submits that Desantis clearly, directly and expressly teaches away from covalently coupled pharmaceutical conjugates of any kind, let alone the topical ophthalmic compositions comprising carriers and the covalently coupled conjugates recited in the present claims. "As a general rule, references that teach away cannot serve to create a prima facie case of obviousness."

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(*McGinley v. Franklin Sports, Inc.* CAFC 8/21/01 citing *In re Gurley*, 31 USPQ2d 1131, (Fed. Cir. 1994)). Thus, applicant submits that Desantis provides no motivation or incentive whatsoever to a person of ordinary skill in the art to modify Desantis or to combine Desantis with Collins for the purpose of making obvious the presently claimed compositions.

Collins discloses a conjugate of an antibiotic, such as amantadine HCl, and a transcobalamin- or intrinsic factor-binding agent (TC- or IF-binding agent, respectively). The TC- or IF-binding agent is an agent that binds to a vitamin B₁₂ transport protein. Thus, Collins discloses that amantadine HCl is one of many potential therapeutic agents, that may be coupled to a TC- or IF-binding agent.

Collins does not disclose, teach, or suggest the present invention. For example, Collins, like Desantis, does not disclose, teach, or even suggest a topical ophthalmic composition comprising a carrier and a conjugate which comprises a therapeutic component covalently coupled to an efficacy enhancing component having the chemical formula A recited in the present claims, let alone such a composition which is effective in delivering the conjugate to a posterior portion of an eye when topically administered to the eye, as recited in the present claims. As discussed above, the amantadine HCl disclosed by Collins is a therapeutic component, not an efficacy enhancing component. In addition, Collins does not disclose, teach, or even suggest why a person of ordinary skill in the art might choose amantadine HCl from the lengthy list of potential antibiotics disclosed by Collins to couple to the TC- or IF-binding agent.

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Moreover, the TC- or IF-binding agent disclosed by Collins has a completely different and distinct chemical structure than the efficacy enhancing component recited in the present claims. The chemical structure of the TC- or IF-binding agent is shown at page 39 of Collins. Thus, the TC- or IF-binding agent disclosed by Collins and the efficacy enhancing component recited in the present claims are both structurally and functionally different and distinct, one from the other.

The Office Action states that 1-Aminoadamantane analogues such as memantine are established in the prior art as useful agents for conjugation with poorly soluble drugs. However, the Office Action fails to identify a prior art reference to support such a position.

As discussed above, Collins discloses amantadine HCl as one of many potential therapeutic components, and does not teach that amantidine HCl is useful in conjugation with poorly soluble drugs. In fact, Collins discloses that amantadine HCl is only one of more than 100 different potential antibiotic agents that may be conjugated to the TC- or IF-binding agent. Moreover, Collins discloses that the amantadine HCl is the agent that is poorly soluble and may benefit from conjugation to the TC- or IF-binding agent.

Applicant submits that the prior art fails to provide a clear and particular showing that one of ordinary skill in the art would have been motivated to combine the deficient teachings of Desantis and Collins for any purpose, let alone to combine them and obtain the presently claimed compositions.

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Simply put, the brief mention at page 92 of Collins of amantadine HCl in a long list of other, different antibiotic agents, is insufficient for Collins, alone or in any combination with Desantis, to teach or even suggest the topical ophthalmic compositions comprising carriers and the covalently coupled conjugates recited in the presently rejected claims. For example, the brief mention of amantadine HCl is insufficient for Collins, alone, or in combination with Desantis, to teach or even suggest a topical ophthalmic composition comprising a carrier and a conjugate which comprises an ophthalmically useful therapeutic component covalently coupled to an efficacy enhancing component having the formula A as recited in the present claims, which composition is effective in delivering the conjugate to a posterior portion of an eye when topically administered to the eye, as recited in the present claims.

Desantis and Collins are substantially different and distinct one from the other. For example, as noted above, Desantis discloses two separate compounds, in two separate compositions, administered by two separate routes. Collins discloses conjugates other than the conjugates recited in the present claims. Thus, Desantis and Collins are directly contrary to each other. Moreover, as noted above, neither Desantis nor Collins even suggest a topical ophthalmic composition comprising a carrier and a covalently coupled conjugate as recited in the present claims which composition is effective, when topically administered to an eye, in delivering the conjugate to a posterior segment of the eye, as recited in the present claims. Applicant submits that there is no proper basis for combining the different and distinct teachings of Desantis and Collins for any purpose, let alone for the purpose of making obvious the present claims.

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Only after knowing of applicant's disclosure and invention would one of ordinary skill in the art even attempt to mechanically pick and choose from among the contrary teachings of Desantis and Collins, while ignoring other teachings of the references and the fact that the references are simply not combinable, and obtain the present invention. Simply put, such hindsight, piece-meal reconstruction of the prior art in view of applicant's own disclosure and invention is an improper basis for rejecting patent claims in general, and the present claims in particular.

In view of the above, applicant submits that claims 1-6, 8, 9, 11, 12, 15 and 16 are unobvious from and patentable over both Desantis and Collins under 35 USC 103(a).

In addition, each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present topical ophthalmic compositions including the additional feature or features recited in any of the present dependent claims. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

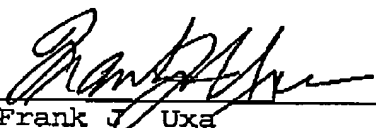
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Conclusion

In conclusion, applicant has shown that the present **claims** satisfy the requirements of 35 U.S.C. § 112, and are **unobvious** from and patentable over the prior art under 35 U.S.C. §§ 103. Therefore, applicant submits that the present claims, that is claims 1-12 and 14-16 are allowable. Therefore, applicant respectfully requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Respectfully submitted,

Date: 2/18/05


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